Drug Development in the 21st Century: The Role of OND

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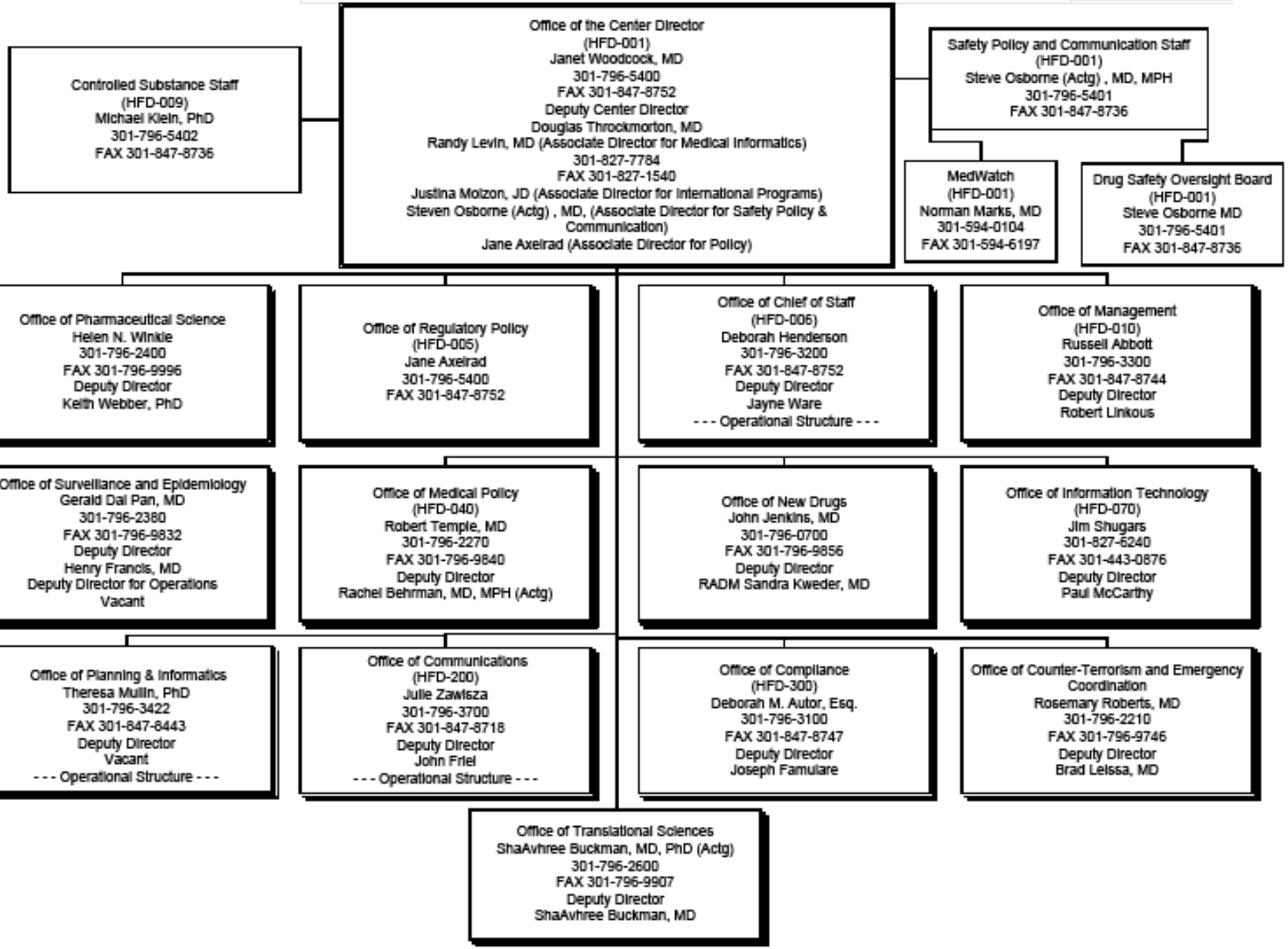
Topics for discussion

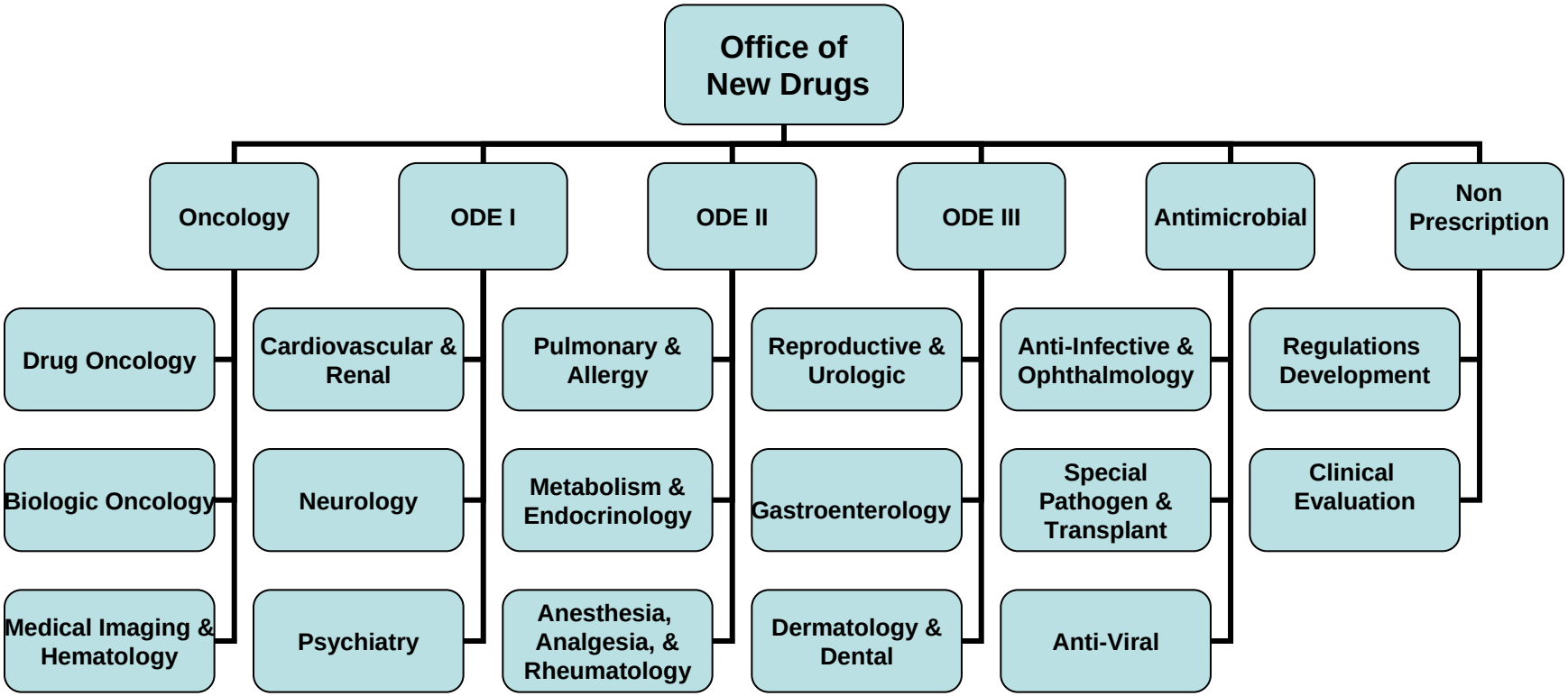
- CDER's and OND's organizational structures
- Phases of Drug Development
- OND's role in the review process
- OND's interactions with regulated industry
- 21st Century Review Process
- OND-led programs and initiatives

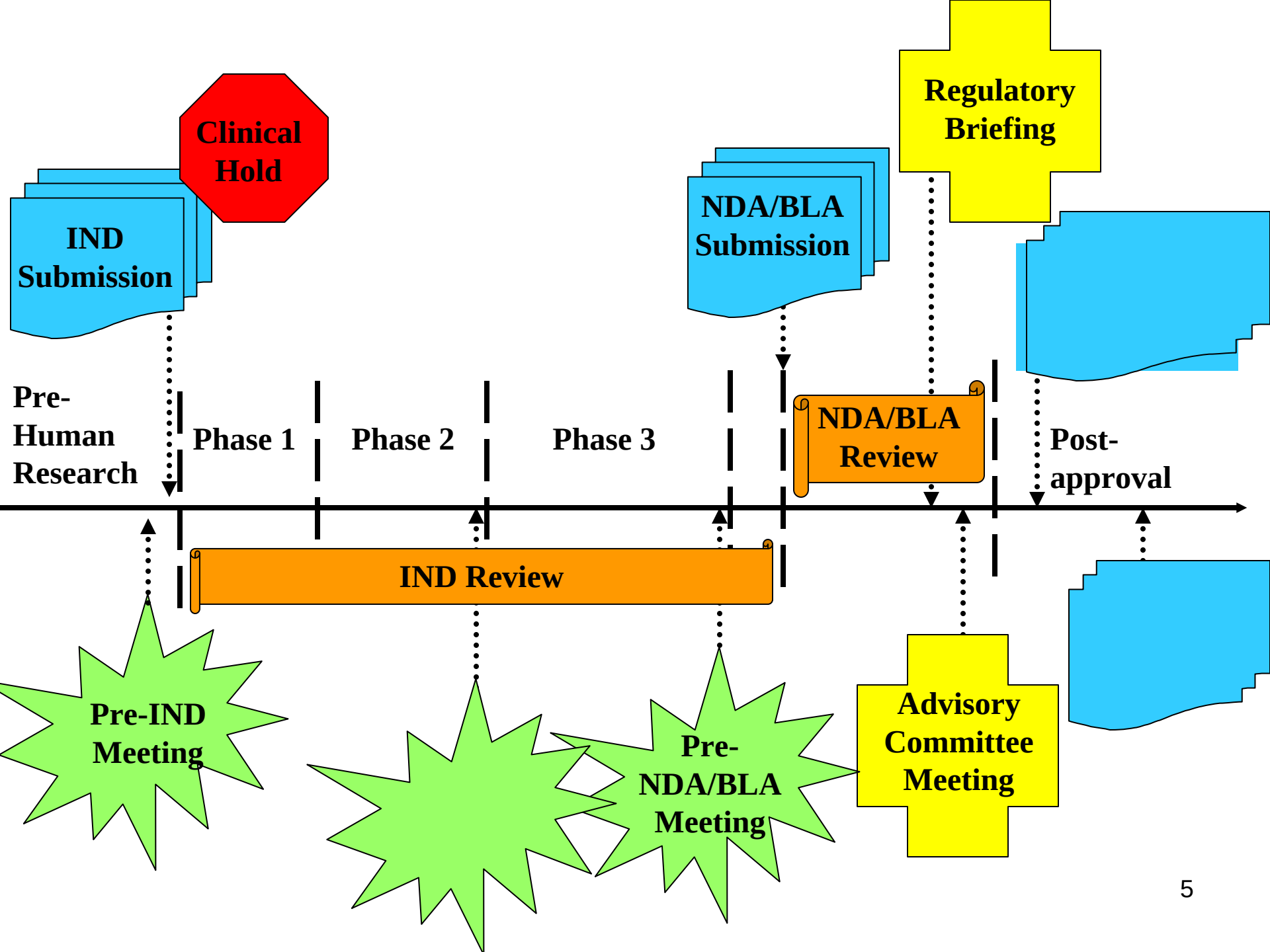
CENTER FOR DRUG EVALUATION AND RESEARCH

March 5th 2009



Office of New Drugs (OND)




Clinical Hold
IND Submission
NDA/BLA Submission
Regulatory Briefing
Pre-Human Research
Phase 1
Phase 2
Phase 3
NDA/BLA Review
Post-approval
IND Review
Pre-IND Meeting
Pre-NDA/BLA Meeting
Advisory Committee Meeting

Scientific Review Team

- *Clinical** (M.D.)
- *Pharmacology/Toxicology** (Ph.D.)
- *Regulatory Project Management** (R.N., Pharm.D., B.S.)
- *Chemistry* (Ph.D.)
- *Clinical Pharmacology* (Ph.D., Pharm.D.)
- *Statistics* (Ph.D.)

* OND staff

The role of OND in the review process

- Provide advice and guidance to regulated industry during drug development
- Signatory authority for regulatory decisions related to new (i.e., not generic) drugs
  - Working in conjunction with the other offices within CDER
- Establish policy and procedures governing the above

Interactions with regulated industry

Why are interactions important?

Communication between

the Agency and industry

facilitates a common goal –

more efficient drug development.

Procedures for meetings

- Meetings can be requested by industry or by FDA
- Meeting requests from industry should be submitted in writing
- Relevant background in the written request
  - ***Guidance for Industry, Formal Meetings with Sponsors and Applicants for PDUFA Products***

Procedures for meetings (cont.)

- CDER will respond to a written meeting request (granted/denied)
- Meeting Types:
  - Type A: stalled drug development program
    - Goal: 14-days to respond (granted/denied)
  - Type B: “milestone meetings” (pre-IND, end of Phase 1, end of Phase 2/pre-Phase 3, pre-NDA/BLA)
    - Goal: 21-days to respond (granted/denied)
  - Type C: all others
    - Goal: 21-days to respond (granted/denied)

Procedures for meetings (cont.)

- Meetings are scheduled to be held within a set number of days from receipt of the meeting request based on meeting type
  - Type A: 30 days
  - Type B: 60 days
  - Type C: 75 days

Procedures for meetings (cont.)

- Background packages are due 2 weeks prior to a Type A meeting, 1 month prior to Type B or C meetings
- Background package content needs to support intended objectives
- Internal CDER pre-meeting ideally 2-7 days prior to the meeting

Procedures for meetings (cont.)

- Draft/preliminary responses to questions submitted in background package sent 24-48 hours before meeting
- CDER will generate meeting minutes within 30 days of the meeting
  - CDER version is the official version: industry is advised to submit disagreements in writing
  - Minutes are not transcripts of the meeting but contain discussion summaries, decisions, and action items

Other interactions

- Written advice, including special protocol assessments, during development
- Labeling, risk management, postmarketing requirement/commitment discussions during application review
- Advisory Committee meetings
- Workshops and public dialogues on policy development (e.g., adaptive trial design)

21st Century Review

- Operationalize Good Review Management Practices and Principles (GRMPP) Guidance (2005)

"The goal of the 21st Century Review is to make the new drug review process more organized, with a more integrated level of management that allows sufficient time at the end of the process to be sure all concerns have been heard and addressed by the decision makers. To help achieve this goal, members of the review team should plan to begin their review as soon as an application comes in the door."

- Janet Woodcock

21st Century Review

- Pilot program in FY 08 to refine the process, one application per OND division
- The new process is a CDER process; all disciplines are expected to follow it for all applications and supplements
- Timelines for this process are being implemented as follows:
  - Original BLA and NME NDAs beginning FY09
  - Efficacy supplements for new or expanded indications beginning FY10
  - All BLAs and NDAs beginning FY11
  - All efficacy supplements beginning FY12

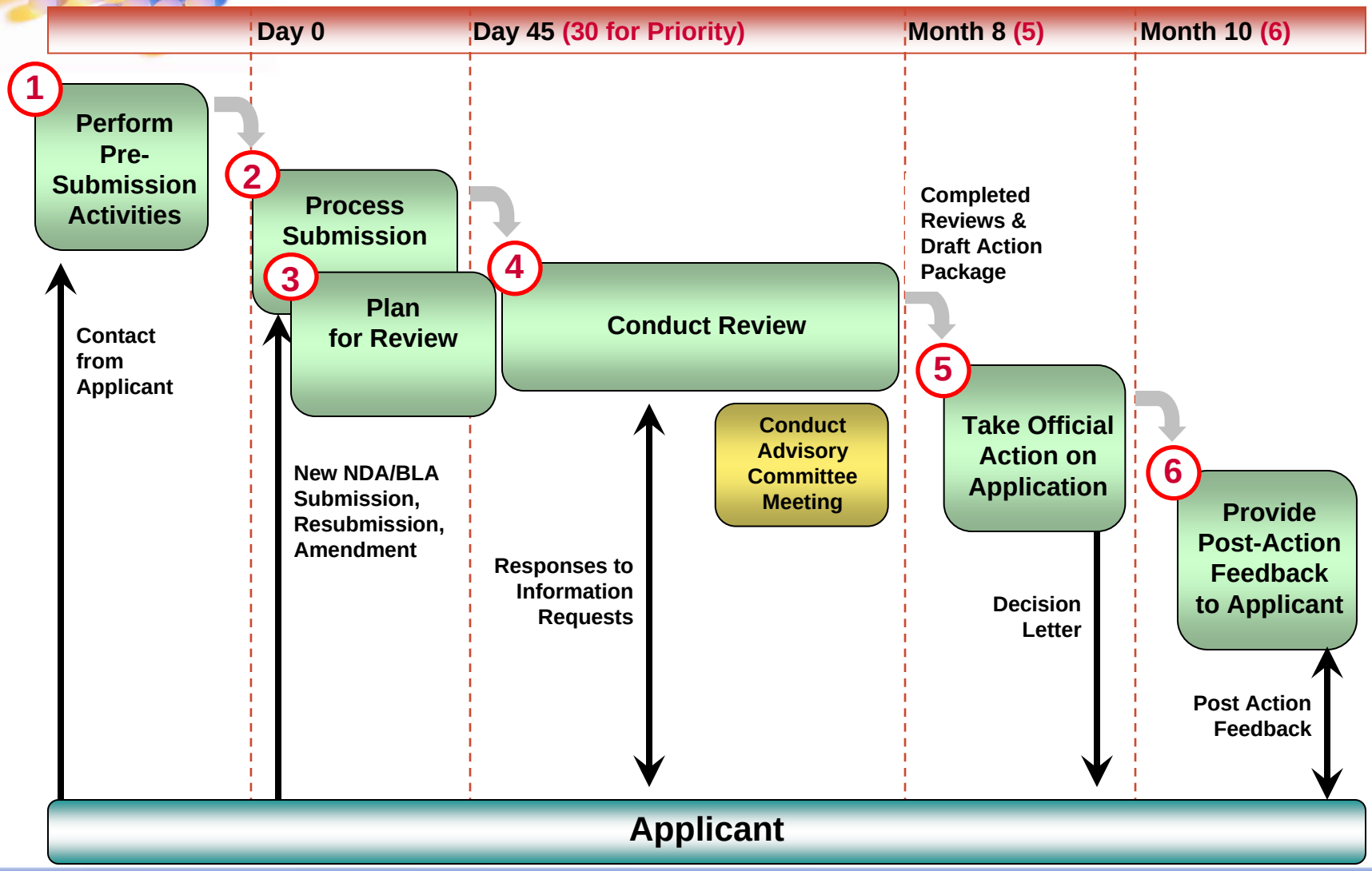
Major Changes in Process

- Optimal teamwork and collaboration across disciplines – to fully exemplify Equal Voice
- Upfront planning with clearly identified expectations
- New pre-submission and post-action activities to educate sponsors and help FDA plan for the review
- Better management of the process
  - Identify and address showstoppers early
  - Defined roles, responsibilities for managing the review
  - Increased interaction between disciplines
  - Structured timeline for review

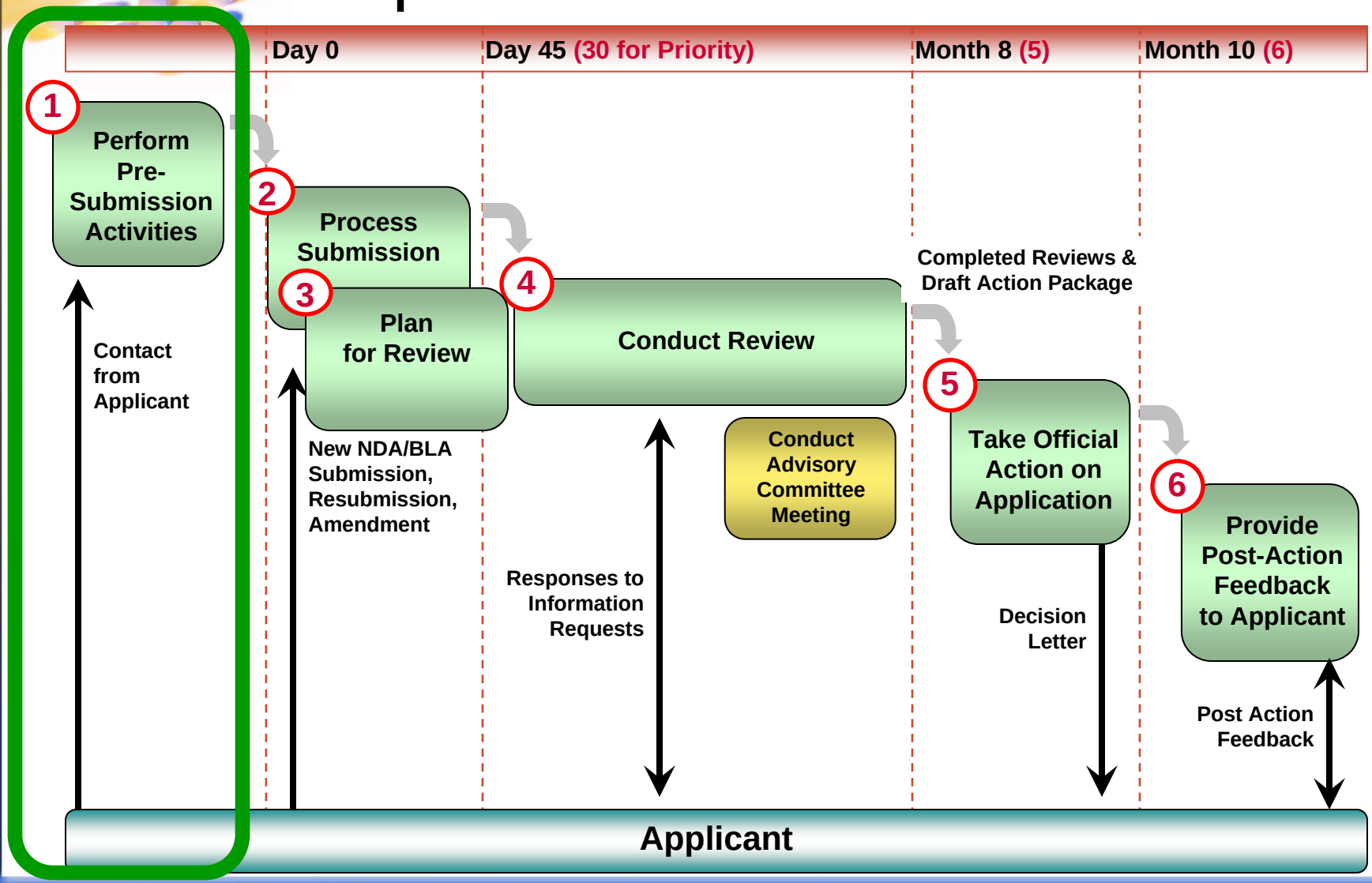
Roles and Responsibilities

- Primary Reviewer – each discipline
- Team Leader – Secondary Reviewer
- Cross-Discipline Team Leader (CDTL)
- Regulatory Project Manager
- OND Division Directors
- Signatory Authority
- Discipline-specific Management

The New 6-Step Process



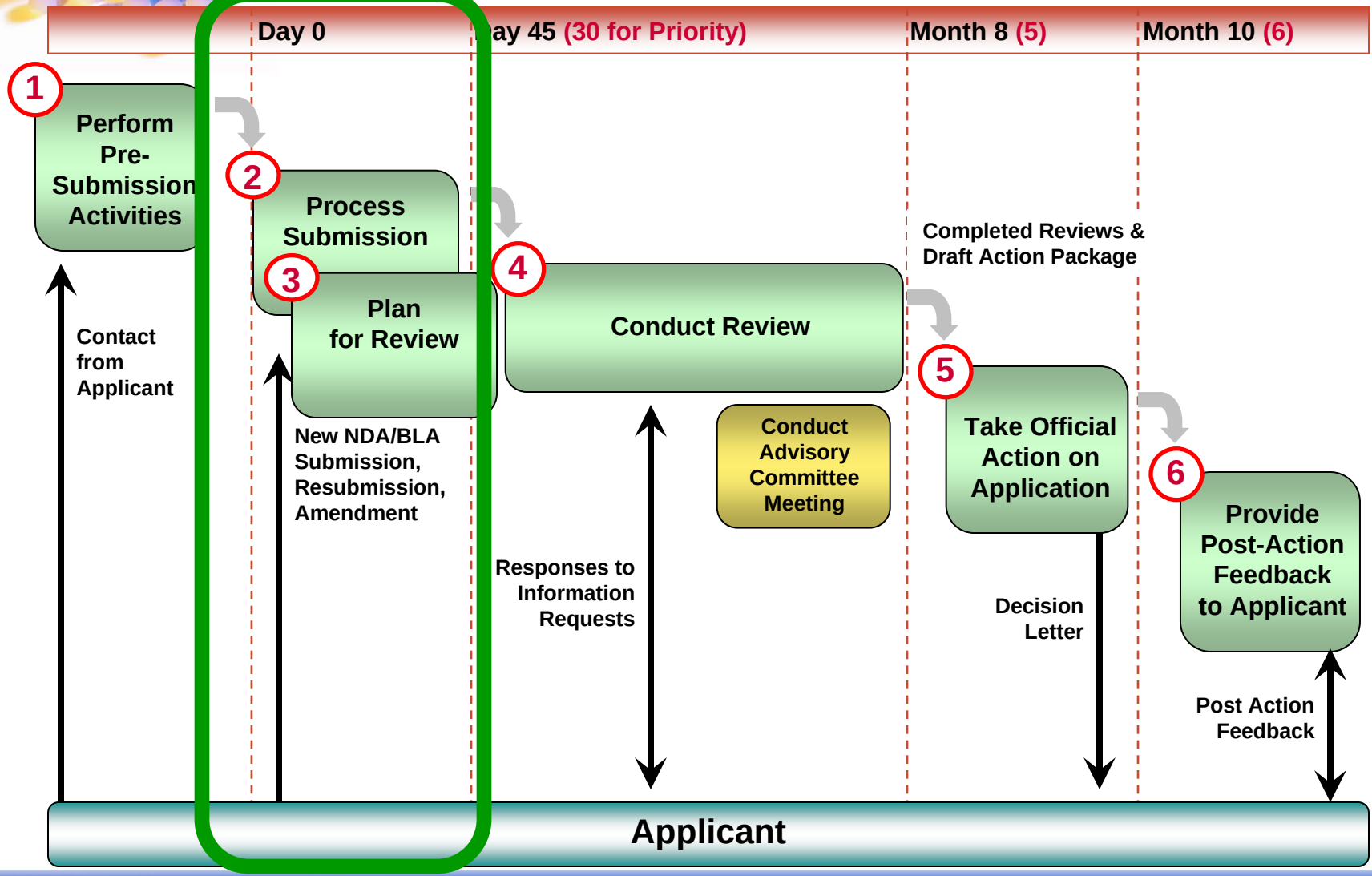
Step 1: Pre-Submission Activities



Step 1 - Highlights

- Pre-NDA/BLA meetings
  - Discuss content/format of application
  - Discuss need for AC meeting
  - Discuss potential REMS and PM surveillance
- Pre-electronic submission meeting
  - Test technology – navigation, formatting, location of datasets
  - Held within 30-60 days of anticipated submission

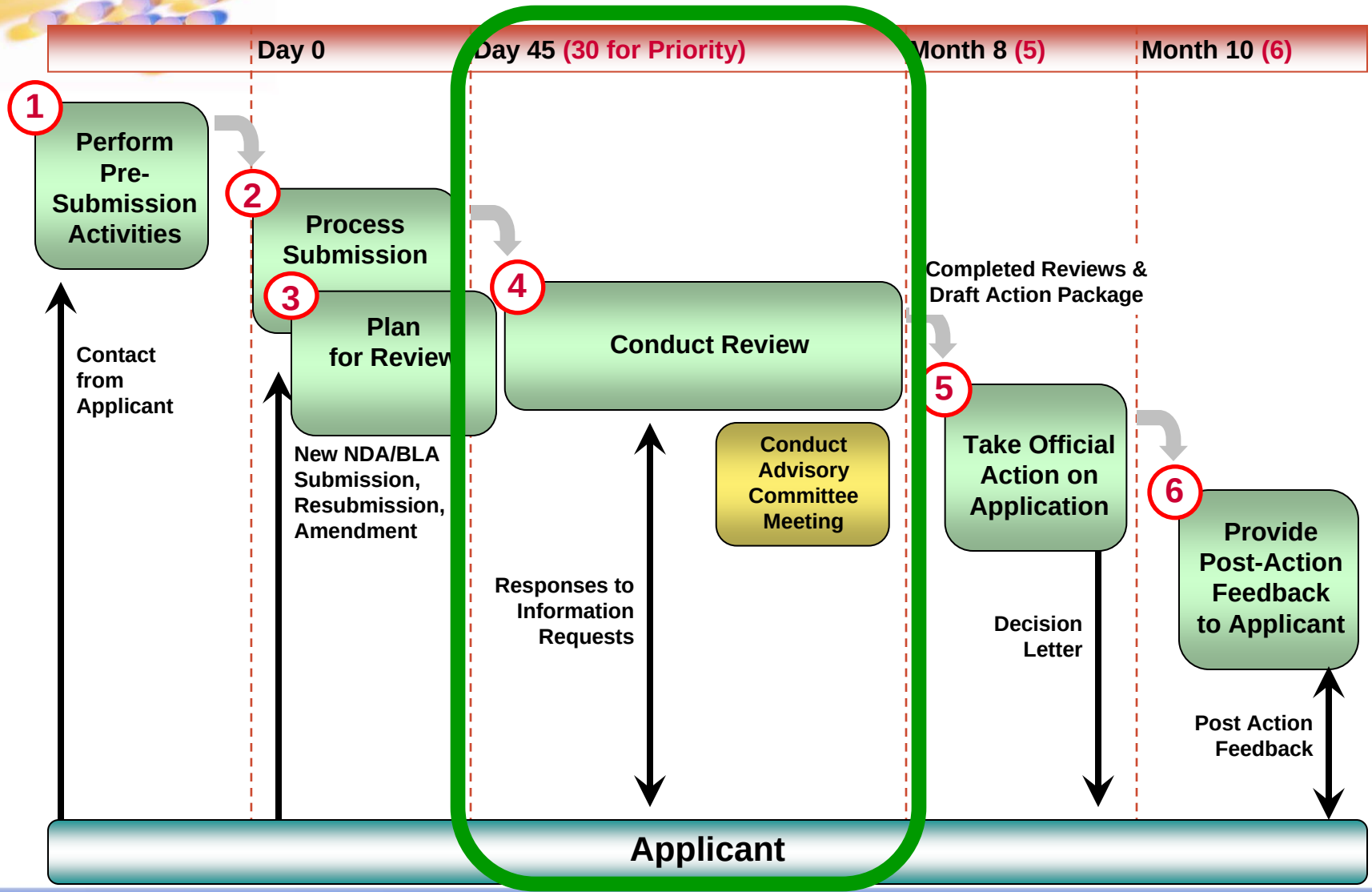
Steps 2 & 3: Process Submission and Plan for Review



Step 2/3 - Highlights

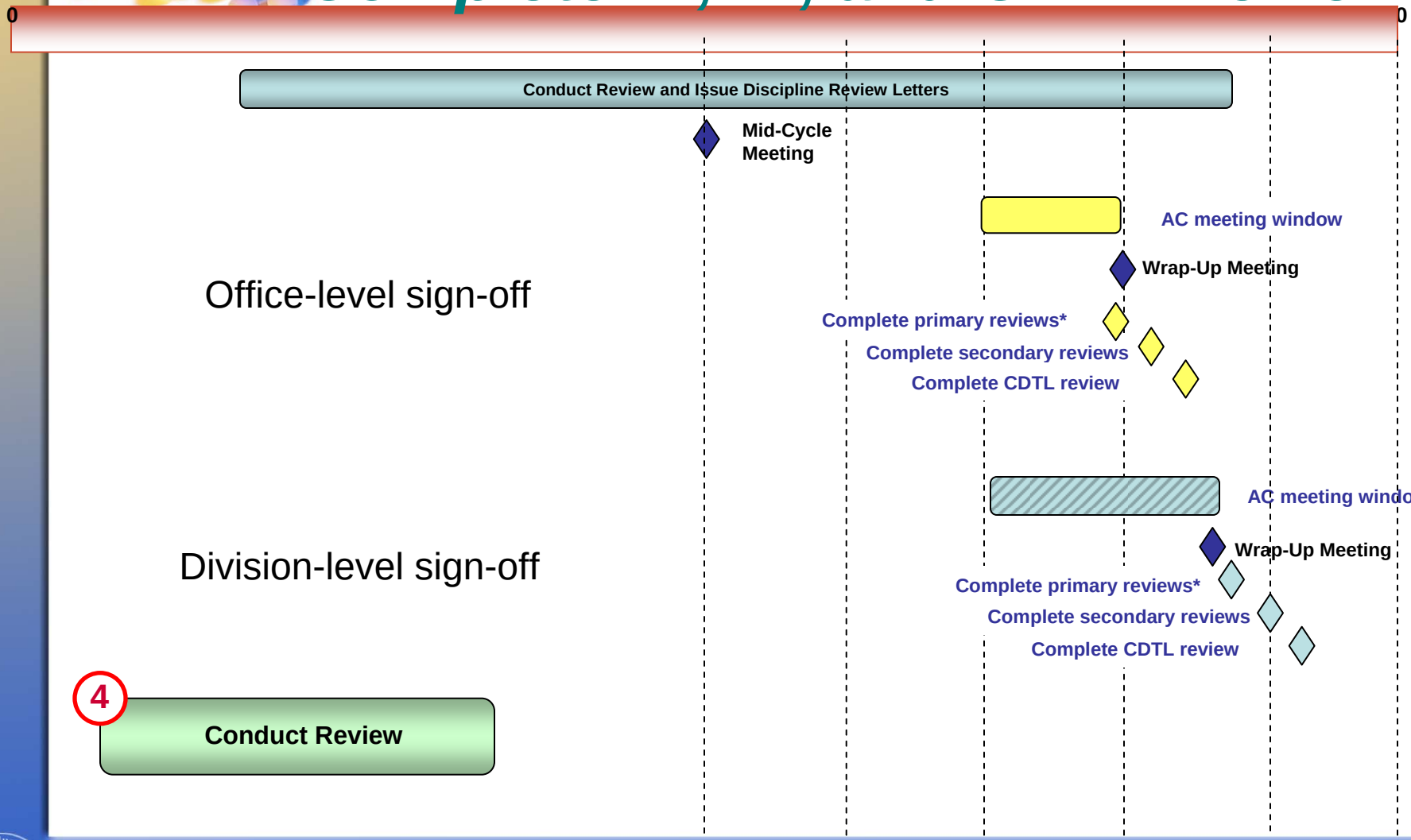
- Review team members assigned
  - CDTL appointed
- Priority/standard review decision (by day 14)
- Conduct filing review using discipline-specific checklists/templates
- Filing meeting (by day 45 (S), day 30 (P))
  - Labeling review for high-level issues
  - Identify RTF issues, if any
- Communicate filing deficiencies and review timeline via 74-day letter

Step 4: Conduct the Review



Step 4: Conduct Review

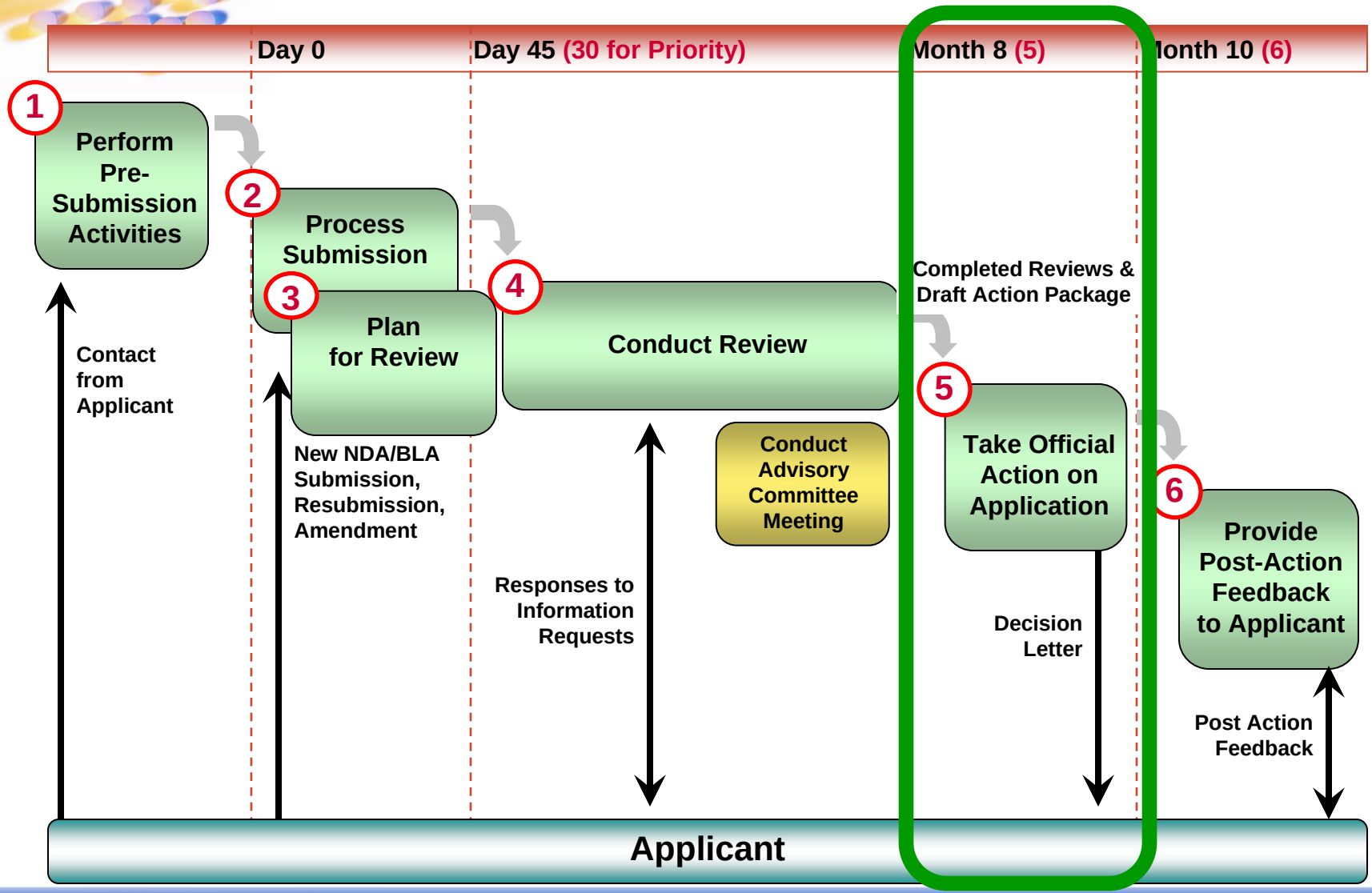
Complete 1°, 2°, and CDTL Reviews



Step 4 - Highlights

- Primary reviewers consult with fellow team members and team leaders
- Mid-cycle meeting (mo 5 (S), mo 3 (P))
- Communicate deficiencies to applicant
- Complete 1º, 2°, and CDTL reviews
- Advisory Committee Meetings (by mo 8 (S), mo 5 (P))
- Initiate internal labeling, PMR/PMC discussions

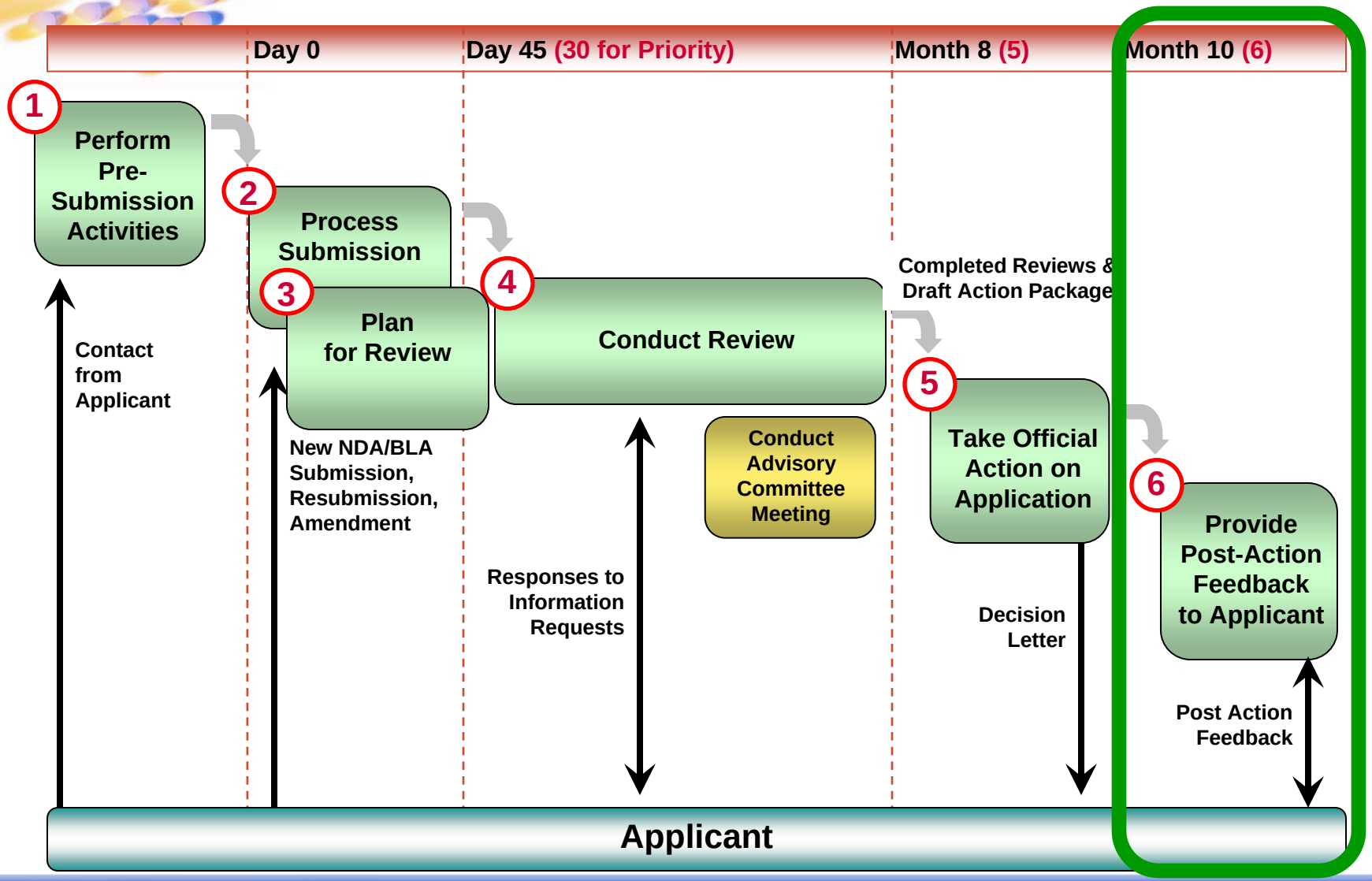
Step 5: Take Official Action



Step 5 - Highlights

- Wrap-up meeting (end of mo 8 (S), mo 5 (P))
  - Reviewers present outstanding issues
  - More detailed labeling discussion
  - Safety issues
  - PMRs/PMCs
- Completion of reviews (CDTL and Div/ODE Dir memos)

Step 6: Post-Action Feedback



Step 6 - Highlights

- Lessons-learned feedback meeting
  - Held for all NMEs
  - Invite applicants
  - Quality checklists

21st Century Review: Summary Points

- Start planning, review, and collaboration early
  - Applications are to be “complete” when submitted
  - Think about need for AC, known PMR/PMCs, REMS at pre-submission. Discuss high-level labeling issues at filing
  - Plan both team and individual reviews, including interim deliverables
- Team works internally on labeling, PMRs/PMCs, & REMS during 4 weeks before 1° review completion
- Key meetings (filing/planning, mid-cycle, wrap-up, feedback) are part of a structured process to facilitate management input and minimize last minute issues & problems
- Feedback at the end:
  - Signatory Authority explains basis of decision
  - Review Team debriefs with applicant regarding the application quality and review process

OND-led programs and initiatives

- Guidance and Policy
- Pediatric and Maternal Health
- Pharmacology/Toxicology
- Regulatory Affairs
- Study Endpoints and Label Development

Guidance and Policy Team

- Aid in the development and implementation of review policies and procedures within OND to ensure a clear, consistent, efficient, and standardized new drug review process (including development, review and clearance)
- Oversight of PDUFA-mandated activities
- Facilitation of OND-jurisdictional matters

Pediatric and Maternal Health Staff

- Implementation of pediatric and maternal health policy and procedures designed to promote the study of drug and biological products in the pediatric population and improve pregnancy and lactation-related information in product labeling
- Consultative services to OND, CDER and FDA

Pharmacology/Toxicology

- Pharmacology and Toxicology reviewers evaluate nonclinical data to aid in:
  - Selecting safe starting and stopping doses for “first in man” clinical trials
  - Identifying potential toxicities that should be monitored in the clinic
  - Assessing toxicities that cannot be addressed in clinical trials such as potential for carcinogenicity, teratogenicity, mutagenicity and chronic toxicity

Regulatory Affairs Team

- Provide regulatory and project management support to the Office of New Drugs, Immediate Office, and to lead various OND and Center-wide initiatives
  - Postmarketing Requirement/Commitment Program (PMR/PMC)
  - Formal Dispute Resolution (FDR)
  - 505(b)(2) applications
  - Biologics expertise

Study Endpoints and Label Development Team

- Oversees quality initiatives and provides expert consultative services in labeling development:
  - Physician's Labeling Rule (PLR)
  - Structured Product Labeling (SPL)
- …and study endpoints:
  - Patient reported outcomes (PRO)

Other initiatives

- Postmarketing safety
  - FDAAA implementation
  - Safety First/Safe Use initiatives
  - Associate Directors for Safety and Safety Regulatory Project Managers roles within each division to coordinate activities

Contact Information

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Questions?